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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/667,556	09/22/00	BURGER A	016779/0154

HM12/1106

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EXAMINER	
FOLEY,S	
ART UNIT	PAPER NUMBER
1648	10

DATE MAILED: 11/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Offic Action Summary	Application No. 09/667,556	Applicant(s) BURGER ET AL.	
	Examiner Shanon A. Foley	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant has cancelled claims 1-15 and added new claims 16-57.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19, 23-28, 40-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 recites the limitation "medicament" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claims 23-28 and 40-57 are vague and indefinite because it cannot be discerned what is intended by a "deleted" L1 or E protein. The metes and bounds of the deleted portions comprising a number of amino acids from each of the L or E proteins are indefinite. It is suggested that applicant incorporate specific amino acid positions to be deleted into the claims found on page 7, line 27- page 8, line 12 to more clearly indicate the portions within the proteins that are to be deleted.

Claim 53 recites the limitation "medicament" in line 2. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-28 and 40-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to deleted or C-terminally deleted L1 or E proteins, or L1 and E which have anywhere from 5 to 55 amino acids have been deleted in unknown portions of the proteins. The specification does not teach what structural elements of these derivations or variants encompass. The specification reduces to practice only two species within the genus, $L1\Delta CE7_{1\text{-}60}$ and $L1\Delta CE7_{1\text{-}55}$. Since the genus embraces a wide variety of possible derivatives and variants of each chimeric polypeptide or protein, the two species are not seen as representative for the full genus claimed.

Claims 16-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant asserts that the references cited in the previous Office action do not provide clinical data adequate to establish a reasonable expectation of success for preventing or treating HPV-specific tumors. On page 13 of the response, applicant cites passages in Muller et al. (Virology. 1997; 234: 93-111) and Hines et al. (Current Opinion in Obstetrics and Gynecology. 1998; 10: 15-19) that clearly indicate concern in the art over the challenges that exist in

papilloma vaccine development. Applicant also supplies additional art demonstrating the unpredictable and uncertain nature regarding the development of human papillomavirus vaccines. Applicant summarizes the teachings of Rudolph et al., which clearly demonstrate the unpredictable nature of the cytotoxic immune response when a single amino acid exchange in virus-like particles is examined. Furthermore, applicant concludes that Toes et al. demonstrate that even if internalization of an antigen occurs, an effective cytotoxic T-cell response cannot be relied upon.

Applicant has convincingly argued that the references cited in the previous action are not enabled. However, applicant has not provided argument or data regarding how the instant composition overcomes the deficiencies in the art regarding human papilloma vaccine development. For example, applicant has supplied art regarding the sensitivity of a single amino acid change in the composition, but broadly claims that any amino acid deletion comprising 5-55 amino acids in any portion of the L1 and E proteins of any human papillomavirus will be effective in treating and preventing any form of HPV-specific tumors. There is no guidance provided by the inventor on how the skilled artisan would be able to make all of the possible chimeric particles that encompass the claimed deletions, while maintaining ameliorative and prophylactic capabilities. On page 21, lines 11 and 12, the specification states that "[v]accination with L1ΔC CVLPs did not protect against the tumour..". The *in vivo* working example include small groups of 3-5 mice that received $L1\Delta CE7_{1\text{-}60}$, $L1\Delta CE7_{1\text{-}55}$, L1ΔC VLP, or buffer followed by challenge with TC-1 syngeneic tumor cells. The TC-1 cells used to challenge the mice would not be realistic to natural exposure since papillomavirus infection is a result of contact with virions. For the preventative working example on page 20, line 29-page 21, line 26,

the data does not suggest that the mice were protected against tumor growth since a delayed onset of tumor growth occurred. Also, the time period of two months would not be indicative of prophylactic effects of the instant composition since papillomavirus dysplasia/carcinoma can develop years after exposure. The treatment working example on page 21, line 28-page 22, line 6, states that all of the mice that received $L1\Delta CE7_{1-60}$ remained tumor-free for two months after the tumor cell injection. There is no data that would indicate that the tumor-free period lasted for a prolonged period of time. Also, due the small number of subjects in each experiment, the results of each are inconclusive.

Therefore, due to the state of the art clearly demonstrating the unpredictability and uncertainty in developing papillomavirus vaccines, the state of the art demonstrating uncertain immune responses to VLPs with single amino acid changes, the breadth of the claims encompassing any deletion in the L1 and E proteins from any papillomavirus ranging from 5-55 amino acids, the lack of skill in the art for making chimeric HPV CVLPs capable of treating and preventing any HPV-tumor, the lack of guidance provided by the inventor illustrating how to make the HPV CVLPs with the desired function of treating and preventing HPV-tumors, the lack of data in the working examples demonstrating treatment or preventative characteristics of the instant composition, it is determined that an undue quantity of experimentation would be required of the skilled artisan to make and use the invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon A. Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on 7:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley/SAF
November 3, 2001

LAURIE SCHEINER
PRIMARY EXAMINER